clusions drawn from these results were at variance with the other physical findings, and, had any great reliance been placed in them, would have led to erroneous results.

There are probably a number of factors responsible for the occurrence of atypical reactions in patients with certified cerebellar tumors. As the more important we may mention first, the great increase in intracranial pressure due to an internal hydrocephalis which ultimately accompanies new growths in the posterior fossa, and second, the diffuse nature of many of the tumors common to the cerebellum.

A CASE OF PRIMARY SPLENIC HODGKIN'S DISEASE.

By Ralph R. Mellon, M.Sc., M.D.

ASSISTANT PROFESSOR OF PHYSICAL DIAGNOSIS, AND DIRECTOR OF THE LABORATORY OF CLINICAL PATHOLOGY, HOMEOPATHIC HOSPITAL, UNIVERSITY OF MICHIGAN, ANN ARBOR, MICHIGAN.

Since 1832, when Hodgkin reported 7 cases of the condition which now bears his name, the etiology has been unknown, and until recently its pathology was ambiguous. But through the efforts of Reed, Longcope, Andrews and others an histological picture has been established which undoubtedly places it among the disease entities and separates it from several conditions with which it has been confused. Most prominent among these are tuberculosis, lymphosarcoma, and pseudoleukemia.

Sternburg,[1] in 1899, held that it was a special glandular form of tuberculosis, just as lupus was a special cutaneous manifestation. This view is no longer tenable in light of the proof that lymphatic tuberculosis and Hodgkin's disease may coexist. At the time this case was autopsied the diphtheroid organism had not been promulgated as the probable cause of the condition. The etiology is far from settled yet. The later results of the vaccine treatment have not given the ground for hope that some of the earlier over-enthusiastic reports afforded.

Characteristically, the disease has its origin in the cervical lymph glands, but cases of anomalous origin have been reported from time to time. Parkes Weber[2] reports a case primary in the bronchial glands. The first signs in this case were cyanosis and edema of the extremities, with osteo-arthropathy as a prominent terminal feature. Symmers[3] reports 2 cases primary in the retroperitoneal lymph nodes, and others having this origin have been reported previously.

---

[1] Ztschr. f. Heilk., 1898, xix, 21.

[2] Proc. Royal Soc. Med., 1909, ii, Clin. Sec., 66.

[3] Arch. Int. Med., 1909, iv, 218.

Lyon[4] states that there is no evidence that a primary splenic form of Hodgkin's disease exists. Reed[5] says that we know of no cases where the pathological anatomy was described in sufficient detail to permit of a positive diagnosis in which the disease commenced elsewhere. Longcope[6] describes a case originating in the retroperitoneal lymph nodes. Simmons[7] also reports 2 cases primary in the retroperitoneal lymph nodes.

But after a thorough search of the literature I am unable to find any case of this disease that can unequivocably be demonstrated to be of primary splenic origin. There are only two which make such a claim, both of which I shall subsequently discuss in connection with the analysis of the findings of this case, which I will now describe in detail.

Case History.—On October 25, 1910, C. L., female, aged seventeen years, entered the University Hospital (Homeopathic). At that time she complained of severe pain in the left hypochondriac region. They were more frequent at the menstrual periods. She had had the diseases of childhood, measles, chicken-pox, etc.

Her present illness dated from February, 1910, when she had chills and fever, with pain in the left side, from which she was in bed for one week. Since then she has had intermittent chills and fever. Her menstruations, which were normal in every respect, began when twelve years of age, but since February, 1910, she has had amenorrhea with vicarious epistaxis. At the time of entering the hospital there was copious epistaxis present every morning, and more rarely through the day.

In September, 1910, she contracted a cold which seemed to settle in the left hypochondrium, causing pain which has been almost constant and accompanied by a persistent cough.

She was first sent to the Gynecological Clinic, when Dr. Kinyon operated for atresia of the vagina, removed cervicovaginal adhesions, and freed an adherent clitoris. Five days after the operation the temperature started to rise, reaching 103.5° on the ninth day after operation, and staying at this point for three days. It then gradually receded, reaching normal in nine days. Previous to this operation the urine was negative and the blood examination was as follows: reds, 4,500,000; whites, 3000; hemoglobin, 90 per cent.

Differential count of leukocytes: Large lymphocytes, 3.3 per cent.; small lymphocytes, 11.7 per cent.; mononuclears, 2 per cent.; polymorphonuclears, 80.5 per cent.; eosinophiles, 2 per cent.; basophiles, 0.5 per cent.; myelocytes, none; count of 400 cells, 100 per cent.

On November 8, 1910, the count was: reds, 2,800,000; whites,

---

[4] Osler's Modern Medicine, p. 675.

[5] Johns Hopkin's Hosp. Rep., 1902, x, 133.

[6] Bulletin Ayer Clinical Laboratory, Pennsylvania Hospital, 1903, vol. i-iv.

[7] Jour. Med. Research, 1903, ix, 328.

1000; hemoglobin, 75 per cent. Differential count: small lymphocytes, 11 per cent.; large lymphocytes, 2.5 per cent.; mononuclears, 1.5 per cent.; polymorphonuclears, 84 per cent.; eosinophiles, 1 per cent. myelocytes, none; count of 500 cells, 100 per cent.

On November 15, 1910, the count was: reds, 2,600,000; whites, 800; hemoglobin, 60 per cent. The differential was in substance the same as the above. The urine was still negative, and a von Pirquet test was also negative after ninety-eight hours.

On November 15 she was transferred to the Surgical Clinic, when she came under the care of Dr. Dean T. Smith. A physical examination showed an enlarged spleen and bilateral enlargement of the inguinal lymph nodes. The axillary glands as well as the cervical were negative. There was an area of dulness over the left lung, extending to the third rib in the sternal line, and going slightly higher in the midaxillary line. Over this area the voice sounds and tactile fremitus were absent, but distant bronchial breathing was noticeable.

On November 18, 1910, Dr. Smith performed a splenectomy, the patient reacting nicely. On the second day following the operation the temperature started to rise, and on November 24 had reached 104°. Up until this time the pulse had stayed with the temperature, but at this point they parted, the pulse going up to 150 and the temperature gradually falling to 100° on November 30, at which time the patient died. The blood count showed: reds, 2,900,000; whites, 11,500; hemoglobin, 70 per cent. Differential count was not materially altered from the other counts.

AUTOPSY PROTOCOL. *External Examination, General.* Build: Frame small; length, 150 cm. Eyes: Blue, eyeball gray; pupils dilated. Neck: Negative. Abdomen: Oval above the level of the ribs. Anomalies: None on external examination. Surgical wounds: 3 cm. to left of ensiform and one finger-breadth below rib is a surgical wound 19 cm. long. The uppermost 11 cm. has stitches and is not united. The rest of the wound is united superficially except at the lower part, where 8 cm. is open. Scars: Scar on forehead above eyebrows. Skin: Pigmentation slight. Hair: Light in color, small in amount; pubic hair shaved. Teeth: Good. Mucous membranes: Pale; conjunctivæ pale. Muscles: Slight muscular development. Rigor mortis: In jaw. Panniculus: Moderate in amount. Edema: Slight edema above ankles. Body heat: Present. Hypostasis: Purple hypostasis on buttocks and back. Inguinal lymph nodes large and palpable. Cervical and axillary lymph nodes not palpable.

Thorax and Abdomen (Main Incision). Panniculus: Moderate amount, 1.5 cm. thick over abdomen. Musculature: Scant in amount, good red color; little blood escapes from incision. Abdominal cavity: Contains about 200 c.c. of clear fluid with fibrin flakes. Small and large intestines distended by gas. Surface moist and shining. Adhesions about coils of intestines and about the cecum; fibrinous exudate. Appendix and cecal region bound down by easily-broken adhesions. Purulent exudate. Appendix points inward to the pelvis, behind uterus. Cecum adherent to the upper border of broad ligament, lying in a walled-off area in which lies a purulent exudate. Parietal peritoneum loosely adherent to the capsule of the liver on right, and capsule more adherent along the upper end of the surgical wound. Omentum: Spread over intestines down to the lower part of the pelvis and adherent loosely to coils of intestine. Congested; vessels dilated; adherent along wound. Position of abdominal organs: Liver four finger-breadths below ensiform at median line, two finger-breadths below rib border on right nipple line. Transverse colon at level of umbilicus. Stomach four finger-breadths above the ensiform. Position of diaphram: Dome of diaphram, fourth rib on right, fifth rib on left. Mammæ: Free from tumor. Gland tissue slight. Right clavicle dislocated at sternoclavicular articulation. Sternum: Negative. Enlarged lymph node at upper end.

Thorax. Thoracic cavity: Left plural cavity contains 1 liter straw-colored fluid; lungs do not recede from wall. Left lung loose adhesions, especially over dome of diaphram and at upper pole. Right lung more adherent at lower margin. No fluid in right pleural cavity. Apex of heart in fifth intercostal space in nipple line. Anterior mediastinum: Fat scant in amount. Thymus: No gross evidence of thymus. Pericardium: Not adherent to epicardium. Fluid not increased, about 5 c.c. clear, straw-colored fluid, no flakes. Heart: On cutting the great vessels there is a large amount of postmorten cruor. Heart size of right fist of the cadaver. Surface shining. No sclerosis. Right heart: Right ventricle contains postmortem clot. Papillary muscles well developed. Left heart: Left ventricle contains a quantity of cruor. Small amount of agonal clot in lower part. Wall, 1.5 cm., 2 to 3 mm. fat. Cardiac orifices and valves: Mitral valve admits two fingers; flaps not thickened; no vegetations. Tricuspid admits two fingers; flaps negative. Pulmonary admits thumb; negative. Aorta admits thumb; flaps negative. Left lung: Lobes separate easily. Surface pale; mottled. Crepitates throughout. Slight anthracosis. On section dry; yield small amount of blood on pressure, less in upper lobe. Lower lobe more fluid and blood and lower portion more firm in consistency. Right lung: Darker on surface; pleura more congested; scattered areas which do not crepitate. Lower lobe is solid and crepitates in upper part of the lower lobe. More blood exudes than from left. On the surface are occasional yellow-white spots which on section are discrete in outline and yield a thick, yellow fluid. Lower lobe: Solid; on section two-thirds is airless and the spaces are filled with creamy mucoid thick fluid. Bronchial glands: Very edematous; enlarged; slight pigmentation.

Abdomen. Peritoneum: Parietal peritoneum shows numerous white spots. At upper pole of wound site was a walled-off area which, when opened, let out a thick, creamy, mucoid fluid, recognized in the gross as pus. Tissues separated at wound site and a handful of clot scraped out. Area of clot and exudate extends over fundus of stomach, clear to esophageal junction. Spleen: Removed previously and in its site blood clots and adhesions of surrounding organs; at site of attachment of spleen the splenic mesentery is drawn up in a knot and still held in place by ligatures not absorbed. Left adrenal: Normal. Left kidney and ureter: Ureter not dilated; perinephritic fat scant in amount: fibrous capsule strips easily; surface smooth; stellate veins moderately distinct. Right adrenal: Normal. Right kidney and ureter: Ureter not dilated; surface smooth; capsule easily stripped; on section, bleeds easily. Duodenum: Admits thumb with ease. Bile passages: No obstruction; on pressure, *very* pale bile escapes. Pancreas: Tail of pancreas adherent to parietal peritoneum. Inguinal and cervical lymph glands were removed; not visibly enlarged.

MICROSCOPIC FINDINGS. Heart: Moderate cloudy swelling with some fatty degeneration.

Lungs: Purulent bronchopneumonia and metastatic abscess. Fibrinopurulent pleurisy.

Liver: Diffuse fatty degeneration. Marked pigmentation of liver cells which consists of bilirubin and hemosiderin. There is also a progressive fibrosis beginning in the islands of Glisson and ramifying between the hepatic cords. The change is almost identical to that found in the lymph glands. The tissue consists of fibroblasts, large endothelial cells, plasma cells, polymorphonuclears, and multinucleated endothelial giant cells.

Spleen: The splenic pulp is almost obliterated by a progressive fibrotic process which varies from an early stage with many fibroblasts to a later stage in which there are very few cellular elements. Intermingled with the fibroblasts are many plasma cells and multinucleated giant cells. Only an occasional Malpighian body is found, which in most cases consists of an artery almost obliterated by proliferative change, while the accompanying lymphocytes are few in number or are replaced by fibroblasts. That the process is quite an old one is shown by the many large areas of anemic necrosis generally diffused throughout the splenic substance. They are surrounded by a great collection of blood pigment giving an intense iron reaction.

Kidney: Generalized cloudy swelling which is more marked in some areas than others. Marked medullary congestion which is also present around the convoluted tubules and glomeruli. At the periphery of these areas the epithelium of the tubules shows a heavy deposit of dark-brown to black granules of pigment of varying size.

Adrenal: Marked cloudy swelling; fatty degeneration; fibrosis and hemorrhage.

Thyroid: Negative.

The cervical lymph glands show slight lymphoid hyperplasia. The inguinal glands show very intense lymphoid hyperplasia, endothelial hyperplasia, great increase in stroma, multinucleated endothelial giant cells but no eosinophiles. The bronchial and retroperitoneal nodes show nearly the same changes, but the fibrosis is more extreme and the lymphoid changes are not so marked. There are many giant cells.

Critical Analysis. An analysis of this case shows that we have a chain of evidence entirely adequate for establishing the anomalous origin of this case of Hodgkin's disease.

1. I wish to lay stress on the fact that at no time in the patient's history has there been any noticeable enlargement of the cervical glands. This is an exceedingly pertinent fact, and in itself is almost conclusive evidence that we must look elsewhere for the origin of the condition.

2. As further evidence for the anomalous origin, we have the patient's first definite symptoms beginning with pain in the left hypochondrium, accompanied by chills and fever. At about the same time, the menstrual flow which had been normal for five years gave place to a vicarious epistaxis. Six months later a cold seemed to aggravate the pain in the left hypochondrium, after which she developed a persistent cough which lasted until her death. This symptom probably corresponded to the involvement of the bronchial glands.

3. Of the lymphatic structures involved by far the most advanced pathological changes were found in the spleen. The practical obliteration of the lymphoid tissue of the splenic pulp by the intense proliferation of the hyalin connective tissue and the many areas of anemic necrosis bore adequate testimony to the age of the condition.

4. The atrophy of the liver, with the extension of the typical Hodgkin's changes into its lymphatics, is further evidence that the splenic changes are very old.

The lack of involvement in most of the nodes in the upper extremities, coupled with the progressive involvement in the other nodes culminating with the very old changes in the spleen, as well as the fact that the events in the clinical history are a reciprocal to this sequence complete the chain of positive evidence that is necessary to establish the origin of the condition in this case.

Wade[9] reports a case the origin of which he interprets to be in the spleen. An abridgement of the findings follow: A farmer, aged fifty-five years, had had several attacks of malaria during his youth. Following a severe cold he developed pain under the left costal margin. In the several months which succeeded the pain moved gradually from this site to the umbilicus. Intermittent chills, fever, and night sweats were a prominent feature. For eight years previous to the attack, which eventuated in operation, the patient suffered from a pain in the right lumbar region. It was learned that he died two years after the operation; nothing more of the subsequent history was learned, nor was any autopsy obtained. An enlarged spleen was removed which showed the picture of Hodgkin's disease. Fibrotic changes were the most prominent, although no areas of necrosis, caseation, or calcification were found. No enlarged abdominal glands were noted at the operation. There was no superficial glandular enlargement. He concludes:

---

[9] Jour. Med. Research, 1913, xii.

"That the spleen was the original site in the case herein presented may be denied on the ground of incomplete assurance of the absence of a focus elsewhere. It is true that without an autopsy at or about the time of operation, this could not be absolutely established, but it would seem that a consideration of the clinical history and of the operation and the microscopic findings indicate definitely that the process arose in this organ."

On physical examination the chest was negative and no superficial glands had been noted. Again, in his conclusions, he says:

"In view of our ignorance of the etiology of the condition, and of the fact that the process occasionally arises in other deep-seated lymphadenoid tissues, the possibility of a splenic origin cannot be denied. Since in this case there was at no time any enlargement of the superficial lymph glands, nor was there evidence of any lymphatic hyperplasia within the mediastinum or abdominal cavity, and since the disease was of long standing in the spleen as evidenced by the gross and histopathological appearance, it should be considered one of primary splenic Hodgkin's disease."

Symmer's case was that of a girl, aged eighteen years, with splenomegaly, who three years before her death from splenectomy passed clots of blood from the bowel and had a chronic relapsing fever. The spleen macroscopically and microscopically showed evidences of Hodgkin's disease, but no place in the description can I find evidence that the changes in the spleen were older than those in the lymph glands. The description states that "no areas of necrosis were found," and the changes in the lymph glands are not recorded because no autopsy was obtainable. He states that at the operation it was not noticed that the abdominal glands were affected, but this statement may also be difficult to prove without the aid of the microscope. He merely states that in his opinion the case represents one of primary splenic Hodgkin's discase, and that he has not been able to find an exactly similar case in the literature.

A review of these cases show that they both fall in the same category, viz., the conjectural. It is true that they are both very suggestive, but the autopsy evidence which makes it possible to unequivocally demonstrate their contention is lacking. In Wade's analysis of his own case he admits that its origin in a focus elsewhere cannot be absolutely disproved without an autopsy, but believes that the case should be called a primary splenic involvement, particularly from lack of evidence of glandular involvement elsewhere, from the clinical history and from the exploratory results of the operation.

When the splenic origin of this condition is so much in doubt the assumption of lack of involvement of all lymphatic nodes on merely gross examination would seem to be taking too much for granted. As the chest was not opened, there is a dearth of evidence regarding the bronchial nodes, and in light of the present theories concerning etiology these nodes would naturally be next in order of involvement. It is a fact not generally recognized that one may have moderate enlargement of glands in one location, which may gradually subside, at which time the progress is usually active elsewhere. This circumstance, coupled with the fact that the inguinal glands in my case, showed moderately-advanced changes, although they were not abnormally palpable, would seem to seriously question the value of Wade's evidence that the lymphatic nodes in his case were not involved.

Another point regarding the clinical history, which he says points very strongly to primary splenic Hodgkin's: "The patient has given no other symptom for years but a pain in the region of the spleen." For eight years before the pain started under the left costal margin the patient suffered from pain in the left lumbar region.

A history of probable splenic trouble covering that length of time with no glandular involvement points much more strongly to a Gaucher type of splenomegaly than to Hodgkin's disease, which does not run such a prolonged course as the former. Under such circumstances I should think that it would be quite necessary to differentiate this condition. The microscopic picture is usually definite, but it must be borne in mind that these changes were superimposed on an old malarial spleen, which might seriously complicate the microscopic picture, especially since fibrosis was the predominating feature.

Conclusions. I am able to find no case in the literature which can be demonstrated to have had its origin in the spleen. The cases of Wade and Symmers are suggestive, but the absence of a complete autopsy render the evidence inconclusive.

I believe that in the case which we have reported we have all the evidence necessary to demonstrate our contention. The entire clinical history covering a period of not over two years, the lymphatic glandular involvement of chest, abdomen, and inguinal regions, all showing changes decidedly younger than those in the spleen, complete a chain of evidence which is entirely adequate.

RESULTS WITH CHOLESTERINIZED ANTIGENS IN NON-SYPHILITIC SERA.

By C. W. McClure, M.D.,

and

E. S. Lott, M.D.

(From the Clinical Laboratory, Department of Internal Medicine, State University of Iowa, Iowa City, Iowa.

That additions of cholesterin to alcoholic extracts used as antigens in the Wassermann reaction increase the delicacy of the test is well established. As small an amount as 0.0125 gram per 100 c.c. of extract sharpens the end reaction.[1]

The specificity of cholesterinized antigens is questioned by many observers. It may be stated that even with those obtaining the best results, certain cases are reported as giving positive reactions which are questionably luetic. These questionable cases and those clinically non-syphilitic cases reported as giving positive reactions can not be placed into definite groups as can those which give non-specific reactions with the non-cholesterinized alcoholic extracts. Therefore, the clinical interpretation of positive results obtained with cholesterinized antigens must be slightly guarded.

Because of this an attempt has been made to find what amounts of cholesterin may be added to an alcoholic extract without decreasing its specificity as an antigen.

Three alcoholic extracts were used: two the livers of luetic feti and one of guinea-pig hearts. The liver extracts were prepared by shaking the finely chopped liver with ten parts of absolute alcohol for four hours on each of three days, placing in the incubator at 38° C. in the interim, decanting, and preserving on ice. The guinea-pig heart extract was made by placing one to two hearts into 500 c.c. of absolute alcohol every week for a period of six months.

The cholesterin additions were made by weighing into a 50 c.c.

---

[1] Loc. cit.